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## Rickets : a history of the changes in the conception of the etiology

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RICKETS

A History of the Changes in the  
Conception of the Etiology

Senior Thesis

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## FOREWORD

In considering a disease, one wants to know: first, how to cure it, and second, how to prevent it.

The cure and prevention in all diseases depends, almost wholly on the conception of etiology. A full understanding of a disease, like that of a nation, depends on one's knowledge of the factors that play a part. Therefore in this paper I have attempted to show the changes in the conception of the Etiology of Rickets, from the first knowledge of the disease down to that of the present.

## RICKETS: A History of the Changes In the Conception of Etiology.

The history of a disease starts with its first clear clinical picture. In the case of rickets we find that this dates from about the middle of the seventeenth century. In 1650 a book by Glissen was published in Latin under the title "De Rachitide sive Morobo Peurili qui vulge The Rickets dicitur, tractus." It was reprinted in 1651 and translated into English by Phil. Armin (1). However, in 1645 Daniel Whistler read as his inaugural address a short treatise on rickets. There is quite a little controversy among authorities as to which was the first to do the original work, but we will not enter that discussion at this place. In any event the recognition of rickets as a clinical entity dates from this period.

To go back and trace a reference to symptoms of rickets in writings of the periods before this is, although very interesting, very difficult. Rickets is a chronic disease with a low mortality and no striking clinical symptoms such as a high fever or prostration, and so might escape the notice of the early writers. One will see that this is not at all an uncommon probability when he remembers that today it is extremely hard to accurately diagnose some of the epidemics that swept over Europe. The same is true of the plagues. As a result there is often an honest but different opinion as to the dis-

ease referred to in the light of our knowledge today. And this is true in spite of the fact that some of the epidemics were very dramatic in their manifestations and clinical symptoms.

In going back to early writings we find that Findlay (2) in searching the archaeological records of Ebers, Brugsch, and London found no clear reference to rickets in any of the medical papyri. Smith(3) says that there is no unmistakable evidence of rickets found in any cemetery in Egypt or Nubia. It is true that Ruffer (4) claims to have found evidence of dental caries in the teeth of all periods of Egyptian history. While caries is often associated with rickets there are other factors which might cause caries of the teeth besides those associated with rickets. Since today we know of the importance of sunshine in the prevention of rickets it is not surprising that rickets should be rare in Egypt if, indeed, it occurred at all.

There seem to be no records of any kind that would lead one to think that they knew of the disease in the ancient civilizations of Babylonia or India (5).

Findlay (6) says that the earliest known example of rickets in man or the lower animals occurred in the ape. He quotes Loret of Lyons as describing the disease in the remains of apes kept captive in one of the temples at Thebes. Findlay himself adds that, "should such be indeed the case it would cause us no surprise, as in modern times young monkeys kept in captivity are liable to develop the rickets". It is true

that the disease may have occurred, and probably did occur in man. But the point he wishes to bring out is that conditions did not at that time exist which would produce the disease as we know it today in our large industrial centers.

Jaeger (7) reports some data on an examination of some bones dating back to the early Middle Ages. He cites the instance of a femur found in a prehistoric grave of the Hallstatt period which showed marked lateral bowing. This evidence might, of course, be disputed, but it is supposed to be supported by three of the eminent pathologists of the day. Part of the difficulty lies in the scarcity of bones of young children of that period.

Garrison (8) states that Delpech thought a description by Thersites in the second Iliad a typical picture of rickets.

When we come down to a later period when Greek civilization was dominating the world, there is still very little to show that the disease was known at that time. Does that mean that they did not have rickets at that time, or only that they did not recognize it? If we assume the latter, it must be that Hippocrates, who was a very careful observer, missed the syndrome. On the other hand some students have found what they consider allusions to rickets in the writings of the man who is known as the Father Of Medicine. Hess (9) gives the translation of the disputed reference as taken from the Loeb Classical Library as follows: "when hump-back occurs in children before the body has completed its growth, the arms and legs attain full size, but the body will not grow correspondingly

at the spine; these parts are defective. And where the hump is above the diaphragm, the ribs do not enlarge in breadth, but forward, and the chest becomes pointed instead of broad; the patients are also short of breath, and hoarse, for the cavities which receive and send out the breath have smaller capacity.....They have also, as a rule, hard and unripened tubercles in the lungs; for the origin of the curvature and contraction is in most cases due to such gatherings, in which the neighboring ligaments take part. Cases where the curvature is below the diaphragm are sometimes complicated with affections of the kidneys and parts of the bladder, and besides there are purulent abscesses in the lumbar region and about the groin, chronic and hard to cure; and neither of these causes resolution of the curvatures". Now if one reads only the first part of this description he might think that writer had the disease rickets in mind. When he reads the last part however it is more likely that Hippocrates was referring to tuberculosis. It is quite probable that there were cases of rickets in Greece at that time but it is likely that the large amount of sunshine in that country would be sufficient to protect the children from the disease. There is also another passage that has been interpreted as referring to rickets: "In some also the attitude assumed in bed contributes conjointly with the malady to produce lateral curvature". He then goes on to add: "these conditions will be spoken of in connection with disease of the lungs". This last would seem to imply that Hippocrates was again thinking of tuberculosis. These passages illustrate

very nicely how easy it is for one to misinterpret older writings.

In " Aphorisms " Hippocrates states: "At the approach of dentition pruritus of the gums, fevers, convulsions, diarrhoea, especially when sutting the teeth, are apt to occur and chiefly in those who are particularly fat and have constipated bowels." We see that both Hippocrates and Galen are very careful observers and give little space to a discussion of diseases of the bones; this would seem to indicate that since neither of these men mention the rickets that the disease did not occur commonly enough to come under their observations(5).

It is in the first part of the second century A. D. before we find the first real account of any disorder that we can say refers to rickets. Soranus of Ephesus, a biographer of Hippocrates and a well known pediatricist and pbstetrician of his day, gives a description of the disease in his book on gynecology and pediatrics, Hess (9) and Findlay (2) both give essentially the same account of the translation of the passage in question. In one chapter, "How must one teach children to sit and to stand?" he gives the following: "When a child attempts to sit or to stand, one must aid its movements. If it sit too early or long, it will tend to become deformed, as the vertebral column bends, due to the softening of the bones. If it stand or walk too soon, the legs (especially the thighs) will become crooked." And again, "Why the majority



of the Roman children are distorted?" "This is observed to happen more in the neighborhood of Rome than in other places. Some suggest as a reason: that the city is undermined by cold waters and that their (i. e. the children's) bodies are easily chilled. Others suggest the frequent sexual intercourse of the women, or intercourse taking place after a drunken bout. The truth of the matter lies in the inexperience of the people with regard to the rearing of children; for women in the city have not so great a love for their children as to have regard to every particular, as the women of purely Greek stock do. If no one oversees the infant his limbs become, in the generality of cases, twisted, for the whole weight of the body rests on the legs, and the floor or pavement on which he walks is hard and unyielding, being for the most part laid with stones. When therefore, he rests upon a hard substance, the weight pressing on the limbs is great, and the limbs which bear him up are frail; the limbs must then of necessity give way a little, since the bones are not yet stiff. Hence, when he first begins to sit he must be propped up with swathings of bandages to counterbalance the ills that gain the mastery over him, nor must he sit for long at first. As he advances further to the stage of creeping and standing up a little, then one should place him up against a wall and leave him alone. But for the purposes of making him approach, use a wheel chair." From this passage we see that it must undoubtedly refer to rickets; and was

very common in Rome. We would expect this to be the case in so much as Rome was a great city at that time, and even today rickets is very common there.

A very interesting phase of this account is the restraining of the free use of the limbs. Soranus in his zeal to aid the growing child did much harm to the child; as is well known today. Because of the wide reputation of Soranus in his field, he left precepts which cause men of the profession to follow this bad practice for years. In the same way, he left erroneous ideas with reference to feeding. Soranus advocates giving the child no food for the first two days; and even then not the mothers milk but that of the nurse. This account might serve as a reminder that the doctor should not do more injury to his patients than he does good.

Rousseau, (5) according to Dick, was the first to attack this bad habit of swathing the infants in bandages as soon as they are born.

W. Ebstein in an interesting historical paper on rickets (10) says that Galen refers to rickets in his work, *De Morborum Causis*". There is a question, here again, as to whether Galen was familiar with the work of Soranus. In either case, Soranus adds a little to the knowledge, for he distinguishes between knock-knee and bow-legs, He also mentions the deformities of the chest, such as funnel-shape and pigeon breast. Galen attributes these deformities to the swaddling of the babies by the nurses in early life. He, especially,

calls attention to it in the case of female babies, and says it was due to the desire of the nurses to make the hips of the girls prominent. Hess (7) mentions a report by Baelz in which there is mention of the same sort of practice found among the Japanese people. The account tells of an encircling deformity below the nipple line produced by pressure of the swaddling clothes upon the soft bones of the infant. Strange as it may seem, he also mentions the excessive nourishment as a factor in producing the deformity.

There seems to be little reference to rickets in the literature until the sixteenth century. But Foote (II) in the "American Journal Disease of Children" mentions some paintings: Stephen Lechner's "Virgin" in 1447 in Colon, "Adoration of the Child" by Hans Bergmaier in 1449, both of which hang in the museum at Richartz; "The Nativity" by Walhgemuts in 1479 at Zwickam; "Virgin And Child" by Hans Bergmaier in 1500 at Nuremberg; these he says are all evidence of the common occurrence of rickets at that time, for the all show the prominent frontal bosses and the groove of the breast or the rosary. Foote argues that since the painters used this type of head for their models that it must have been fairly common.

The man known as the Roman Hippocrates, Celsus, in the Reigns of Augustus and Tiberius, wrote eight books on Medicine. He tells of caries of the bones but does not mention rickets; so we are at liberty to use our own views on the matter as to whether rickets existed in Rome. It is quite

probable that it did, but was not recognized as such, due to the lack of the striking clinical manifestations, which were very much in evidence in most of the diseases that were well known at that time.

Theodosius in the sixteenth century, living at Bologna, mentions the disease in his "Medical Epistles" published about the middle of the century. Hess (7) mentions this account and calls attention to the fact that again it came from Italy. He cautions us not to interpret this as due to the extreme frequency of the disease there; but rather to the position of pre-eminence that Italy held in Medicine at that time. Theodosius tells of being called to see an infant, aged eighteen months, which could not move or sit; indeed could hardly hold its head erect, and which showed in the dorsal region both a gibbus and a marked lateral curvature. He does not tell how common this disease was at that time. Due to the age of the patient there is not much doubt that this was a case of rickets.

Some writers mention an account of rickets written in 1582 by a Swiss physician Reusner. Hess (7) writes that he inquired of several of the large medical libraries, both here and abroad, and was unable to obtain any information concerning it.

Wood Jones (II) writing in 1907 after an extensive study of bodies from Nubia and Egypt found that osteo-arthritis with extensive lipping of the articular surfaces to an extent unknown today. They did not show definite evidence of rickets although the femurs did in some instances show bowing.

Findlay (2) remarks that Ruffer imagined he found rickets in the Soudan, but that Ruffer was not aware of the amount of bowing the normal femur might show. Dick (5) tells of the bones of 4000 people, dating from the thirteenth to the sixteenth century, in an excellent state of preservation, under the church at Hythe, and showing evidence of osteo-arthritis, but no rickets.

In the seventeenth century we find a French physician Guillimeau (12) giving an account of rickets. He writes in "A Treatise of the Disease of Infants and Young Children" published in 1609: "But we must also look and have an eye that the nurse or she that swathes the child and dresses him do not make him worse, and of a well fashioned child, in all the parts of his body, do not make him deformed or misshapen, and so spoil him. For in swathing the child most often they bind him and crush him so hard that they make him grow crooked.....but this crushing makes his ribs and breast stand out, so that they are bended and draw the vertebrae to them, which makes the back bone to bend and give inwardly or outwardly or else to one side; and that causes the child to be crump-shouldered or crooked-breasted, or else to have one of his shoulders ot stand further out than the other. Some also bind the hips so hard that they become small, and that hinders them from growing and waxing big, which doth much harm, especially to maids who should have large hips, that when they come of age they may bring forth goodly children. Galen has observed that the too straight and hard binding or crushing of the hams and legs of little child-

ren when they are swathed, doth make them grow crooked-legged and they will remain, as the Latins call it, Vari or Valgi, growing either inward or outward with their knees. This imperfection may also happen through the nurses fault, by always carrying the child upon one arm, and the same side, and by holding the knees hard toward her and making them stand like a bow." There is not much doubt but that Guilleneau was describing the same syndrome that later was known as rickets.

Pare', another Frenchman, in 1663, (7) a surgeon during Francis I, describes varus and valgus deformities of the legs. He does not refer to active rickets, it is true, but from his accounts the results of rickets were well known in France at that time.

The next reference to rickets takes us to England and a heated argument concerning Whistler and Glisson. In 1645 Whistler published an inaugural address for his Doctor of Medicine, "Inaugural Medical Disputation on the Disease of English Children Which is Popularly Known as Rickets." Hess (7) writes that there is no copy of this in the United States, but that he had the Library of the Surgeon General give him a photostatic copy of it. Hess describes the paper as being terse and direct, of being more like a compendium than a first or early description of a disease. Whistler describes the disease as being endemic in England, but was unknown to the ancients. He says that it had been observed about twenty-six years before this time, and the name rickets given to it by those who treated the disease empirically. The Dorset dialect gives its origin from the verb, to "rucket", meaning to

to breathe with difficulty. He gives seventeen diagnostic symptoms: Swelling of the abdomen, especially on the right side, enlargement of the epiphyses of the joints, nodosities at the costal-condral junctions, general softness of the bones, enlargement of the head when hydro-cephalus supervenes, flaccidity of the soft parts, retarded dentition and caries of the teeth, narrowness of the chest, prominence of the sternum and deformities of the thorax, labored breathing and cough. He also added other symptoms which we recognize as complications of the disease.

Sir Norman More tells us that the original work was done by Glisson and that Whistler stole it (13). Hess (7) and Dick (5) are both of the opinion that Whistler had no intention of trying to steal the efforts of another man. Some writers have suggested that Whistler, since he was only getting his degree at that time, and that Glisson, a well established authority, and a man of forty-eight years, it would have been impossible for Whistler to have hoped to claim the original work. Hess (7) suggests that it was quite likely that a young ambitious student should wish to write on a new and interesting disease upon which so much new and interesting work was being done, and that he probably used some of the experimental work of Glisson's. And it is not likely that Glisson would care if a comparatively unimportant student should want to use some of his material.

Fuller (14) in a paper entitled, "Good Thoughts in Bad Times", published in 1647, wrote of "A New Disease" in the

following way: "There is a disease of infants (and an infant disease having scarcely yet gotten a proper name in Latin) called the rickets; wherein the head waxeth too great, whilst the legs and lower parts wain too little. A woman in the west hath happily, healed many by cauterizing the vein behind the ear".

One year before the work of Glisson appeared, a treatise entitled "De Affectibus Omissis", by Arnold Boate (7), was published, which contained some references to rickets. He describes deformities of both the chest and sternum. He writes "Not only does this disease exist in England and Ireland, but in other regions it is also present, and so far as Gaul is concerned, to my knowledge, it most certainly exists there. Indeed in the space of three and a half years since these things were written I have seen various children here in Paris laboring with the disease, and by these methods familiar to me and by the principles indicated I have happily been able to effect a cure." Three years later he published a book written by his brother. This book was finished in 1645 (15). It contains the following: "Among the reigning diseases of Ireland Rickets also may with good reason be reckoned, and is so well known to everybody in England that it is needless to give any description of it; and yet to this day never any physician, either English or any other nation, made any the least mention of it, no not in those works which are expressly written of all manner of disease and accidents of little children.

"In Ireland this disease is wonderfull rife now, but it



hath nothing né'er been so long known there as in England, either through the unskillfulness or neglect of the physicians (the most part whereof in both kingdoms to this day are ignorant not only of how to cure it, but even of the nature and property thereof ) or that really it is new there, and never before having been in Ireland, hath got footing in it only within these last few years." So it is quite evident that rickets was well known by 1650.

In 1650 Glisson, A Fellow of the Royal College of Physicians of London, brought out the result of his work on the new disease of children. The treatise was published in Latin under the title, "De Rachitide sive Morbo Puerili qui vulgo The Rickets dicitur", and a year later the work appeared in English. Dick (5) says that there were two editions printed in London that year. Originally there were seven members, Fellows of the Royal College, appointed to collaborate in its composition. Glisson, who was an orthopedic surgeon and might have gained his first knowledge of the disease from his observations of the results of rickets, did so much of the work and so far outshadowed the other men that they withdrew in order not to deform the work.

It is interesting to note that several other men made important contributions to our knowledge of science during the same century. Among these were Bacon, Harvey with his important contribution to anatomy of the circulatory system, Newton Browne and Descartes the French physicist.

Galen had thought of the body in terms of the humeral

theory and Glisson was not able to escape this way of considering the body. As an example Glisson writes; that rickets is a cold distemper; that it is moist; that it consisteth in penury or paucity of spirits; that it consisteth in stupefaction of the spirits. Thus we see that the philosophical attitude toward medicine was still in vogue. The bacterial basis for disease had not yet been proven.

Glisson suggested the word "rackitis" from the Greek word meaning spine (5) . In German (7) the disease was called "rackitis" and in French "rackitisme". Dick (5) suggests that the word rickets was in common usage in England when Glisson wrote, and that he adopted the common word. Hess (7) also took this view. Dick also tells of the English word "rick", meaning twist, as the origin of the word.

Glisson was firmly that rickets was a new disease. He writes of it: "This is absolutely a new disease and never described by any of the Ancient or Modern writers in their practical books which are extant at this day, of the Diseases of Infants. But this disease became known as far as we could gather from the relation of others after a sedulus inquiry, about thirty years sines, in the countries of Dorset and Somerset, lying in the western part of England, since which time the observation of it hath been derived from other places, in London, Oxford, Cambridge and almost all of the southern and western parts of the kingdom; in the northern countries this affect is very rarely known, and scarcely yet made known among the vulgar people." (7). While Glisson thought he was deal-

ing with a new disease, yet we have shown that although the disease was not always recognized, still there were evidences of it, as we have shown in above places. And as we now know of the importance of sunlight on the production of rickets, it must have been present before the seventeenth century. Sir Thomas Barlow (15) says that rickets was Coeval with civilization. The evidence, however as we have shown, does bear out the fact that it existed in the ancient civilizations of Babylonia, Egypt, and India. Dick (5) suggests that it would be more accurate to say that it was a disease of modern industrialism of the great crowded towns of Europe. Before that time it was likely only an isolated case, except where conditions simulated these, such as were in the Roman civilization at the time of Soranus of Ephesus. It is true that as far as England was concerned, the disease did appear there about the beginning of the seventeenth century. We see that the crowded towns of northern Europe with their cold damp winters, during which the infant was kept inside for months at a time, and their lack of sunshine plus the tight swaddling, which was almost universal at that time gave a perfect set of conditions to produce rickets. Further, we can understand in the light of the present conception of the causes of rickets, and its prevention, just why the child recovered when he was a little larger and could get out in the sunshine and have plenty of exercise. The first place for an account of rickets to appear was in the "Bills of Mortality" (5&7) where it is given as the cause of a large number of deaths.

While the discussion of the one first to write of rickets can probably not be solved, it is quite possible that neither Glisson nor Whistler used the work of the other. At any rate Glisson's work gives us a description of the clinical syndrome which has been little enlarged upon even today.

Dick (5) gives us a description of Glisson's clinical Syndrome. He makes his anatomical observations under four headings:

" I. Anatomical observations, the body not yet being opened, which are outwardly visible upon the first appearance of the naked body:-

1. An irregularity or disproportion of the parts; namely, the head bigger than ordinary and the face fat and in good constitution in respect of the other parts;
2. The external members and the muscles of the whole body were slender and extenuated, as if it had been wasted with an atrophy or a consumption;
3. The whole skin, both the true and the fleshy and the fattish membranes, appear lank and hanging loose like a glove;
4. About the joints, especially about the wrists and ankles, certain swellings are conspicuous;
5. The articles or joints and the habits of all the external parts are less firm and rigid and more flexible than at another time they are observed to be in death;
6. The breast is outwardly lean and very narrow, especially under the arms, and seemeth on the sides to be, as it were, compressed; the stern also is somewhat pointed like the keel of a ship or the breast of a hen;
7. The top of the ribs, to which the stern is conjoined with gristles, are knotty, like unto the joints of the wrists and ankles;
8. The abdomen is lean, but inwardly in respect to the parts contained in it is somewhat sticking out, and seemeth to be swelled and extended.

II. The abdomen being opened:-

- I. The liver in all that we have dissected hath exceed-

- ed in biggness, but was well coloured, and not much hardened nor contaminated by any other remarkable vice;
2. The spleen for the most part not to be contumed;
  3. We have sometimes espied a wheyish water in the cavity of the abdomen, but, indeed, not often, nor in any great plenty;
  4. The stomach and guts are somewhat more infected with flatulent humours than sound bodies usually are;
  5. The mesentery is sometimes faultless and sometimes affected with glandulous excrescences;
  6. The kidneys, ureters, and bladder, unless there be a concomitancy of some other disease, are laudably sound. We observe in general of all the viscera contained in the abdomen that, although the parts containing them are very much extenuated and emaciated, yet are they as large and as full, if not larger and fuller, than those seen in sound bodies, as has been said of the liver.

### III. The stern being withdrawn.

Various morbid conditions are described, adhesions, enlargement of the mediastinal glands, but Glisson is careful to not say that all the conditions found at post-mortem examinations may not be due to rickets at all.

### IV. The skull being opened.

He notes here that the condition may be complicated with hydrocephalus.

He describes the signs under five heads:

- I. The diagnostic;
- II. Signs which belong to the disproportioned nourishment of the parts;
- III. The signs which belong to the respiration;
- IV. Those that appertain to the vital influx;
- V. Certain vagabond and wandering signs."

The beading of the costal-condral junction and the enlargement of the epiphyseal lines of the long bones, the softening and bowing of the long bones are all described. He gives this picture:- "The younger children who are carried about in their nurses arms when they are pleased with anything do not laugh so heartily, neither do they stir themselves with so much vigor, and shake and brandish their

little joints, as if they were desirous to leap out of their nurses hands; also when they are angered they do not kick so fiercely, neither do they cry with so much fierceness, as those who are in health..... They are not delighted with the agitation of their bodies as other children do; yea, when the disease prevaiileth they are averse to all motion of their limbs, crying as they are at play that is ever so gentle, and being pleased with gentle usage and quiet rest. Their countenances are much more composed and severe than their age would require, as if they were intent and ruminating on some serious matter."

Glisson did not think that rickets was a congenital disease, but a result of the environment. He did, however, think that certain conditions in the parents might render the offspring susceptible, as: "a soft, loose and effeminate constitution of either parent; an over moist and full diet; a delicate life abandoned to ease and voluptuousness; a lack of exercise, immoderate sleep, a sedentery and soft life.... We affirm that the rifestness of the disease in England hath been much promoted by that long and secure peace..... for by this the more wealthy and secure families which were first invaded by this evil, and which still doth invest them more than others, had addicted themselves to idleness and a loose effeminate life, and therefore they fall into a moister, softer and degenerate constitution and such as was less purged and cleansed from excrementitious humours." He thought the disease was more frequent in the south and west than other parts of England, because the life was easier

there, and more fruitful.

It is quite easy for us, with the knowledge which we have concerning the cause of rickets, to see the reason for a lack of adequate treatment; since they had no idea of Vitamin D or of the part played by sunshine in the prevention and treatment of rickets. Glisson advanced many arguments, to us absurd, to show that rickets consisted in "appaucity of spirits" etc. In his clinical and pathological observations he has the trend of modern medicine; but in his etiological conception of rickets he is hopelessly of the past. This is, of course, to be expected when we remember that Glisson lived during this transition period.

Burland (I6) cites a case of rickets and an examination that was made in 1856. In that year, Wilkenson examined the remains of Princess Elizabeth, daughter of King Charles I, who died in 1650. The bones showed evidence of rickets. The epiphyses were definitely longer, the legs bowed out, the spine shaped like a double S and the humeri curved outward. Bad nursing was thought to have been the cause of her death. This is an interesting account in as much as her death occurred the same year that Glisson published his book on rickets.

Mayow (I7) in 1669, published a treatise, "De Rackitide." He added little to the former picture of the disease. He did differ in his idea of the cause however, thinking the pathology was primarily in the muscles and that the bones were sufficiently nourished and the muscles bent the bones

by drawing them shorter. Mayow says, "the Scab or the Itch coming upon this disease confers much to the cure thereof."

The literature of the eighteenth century contains many medical theses written on the subject of rickets, but there is little added to our clinical picture, and most of the writers follow Glisson in his explanation of the causes. The Germans (7) began to call it the English disease and to a large extent still do. Muellen mentions it in connection with scurvy, saying that until recently it had been of rare occurrence, but that the Gallic exiles had brought it into Germany. Camerarius (7) describes rickets in Nuremberg. It deformed even the strongest infants; the ribs being distorted, the abdomen swollen, and respiratory spasms and convulsions were mentioned as common symptoms. He mentions the finding of worms in the stools; and thinks the cause of rickets to be due to the coarseness of the food, the giving of cold water, and the exposure of the bodies of young children to the cold air. Here again we see the importance of the conception of the cause of a disease, upon the treatment of that disease, and the harm that may result from a wrong conception as to the etiology. In the above, the obvious result would be to shield the body of the child, at all times, from the cold air and thus also from the sunlight; and so the child would be unconsciously deprived of one of the most valuable agents in combating rickets.

Boerhave (5) about the beginning of the century gave



as the cause of the disease a venereal poison. A pupil of his, von Swieten, believed this also, and makes the interesting observation that rickets occurred most often in the children of the Spanish and Portuguese Jews living in the ghettos. Portal also believed that rickets was a manifestation of syphilis, and Hess (18) tells us that it is only recently that the French gave up the idea that it was based on syphilis.

The beginning of the nineteenth century brings an interesting account of rickets in the town of Wezlar by Wendelstadt (19) where house after house had its deformed children. He writes, "Rickets is a disease which attacks children only between the ages of one and two years. According to our custom they are fed with pap and starch even while in swaddling clothes; as much is put in as can be forced down." "If the children could go about the streets and country all might go along without much damage.....but as this is not the case but as just the children must sit indoors, their digestion suffers severely.....which ends in death, or if they continue to live, they develop thick joints, cease to be able to walk or have deformed legs."

Trousseau (20) in the same century, showed the relation of rickets and osteomalacia. A little later, a German, Elsasser, mentioned the softening of the cranial bones, one of the few points added to the clinical picture since Glisson. This was followed by the seasonal incidence of the disease noticed by Kassowitz of Vienna; which was to prove of great value in working out the relation of sunlight as a therapeutic

agent by later workers (7).

In the nineteenth century Pommer, 1885 (21), contributed to the understanding of rickets with his work on the histological pathology. Little (22) about the same time wrote a paper concerning the medical and surgical aspects of genu-valgus. Fagge, of Hythe, England, was the editor of Guy's Hospital Reports and a very able pathologist. In 1880, he made some investigations of rickets and cretinism. These experiments helped greatly in clearing the confusion of these two disease (23).

Up until 1880 we find that the medical profession accepted the views of Glisson as to the etiology of rickets. But men were beginning to question these viewpoints, and to experiment with diets and hygienic factors, for these were the two most popular theories explaining the cause of rickets. The hygienic theory has been supported by Palm (1890, who called attention to the importance of sunlight (24). Kassowitz (1921), von Hansemann (1906) and Findlay (1908) also supported this view. Diet as the causative agent was adhered to by Cheadle (1906), Sutton (1907), Still (1905) and an intermediate position was taken by Cautlry (1913), Holt (1918), Howland (1918), and Sweet (1921). These latter men said that diet and hygiene both were important factors in the etiology of rickets. Stoelzner (1900) said rickets was due to a disorder of the adrenal gland. Basch (1906), Klose and Voit (1910) and Matti (1913) thought it due to disorder of the thymus. Edheim (1914) said the parathyroid was responsible. Later in-

investigators were unable to prove any of these theories of glandular disturbances as the causative agent however.

Pritchard (24) went back to a theory of Heitzman's (1873) and in 1911 said that long standing cases of acidosis lead to a calcium deficiency which resulted in rickets. Morpurgo (1900) and Kock (1911) placed rickets on an infective basis. Kock injected bacteria into puppies and produced what he thought was rickets, but which other experimenters was only a disturbance of the calcium metabolism due to the hyperpyrexia produced (25).

In the second decade of the twentieth century there began a new interest in experimental medicine and many investigators turned to the causative agents of rickets. Kornechevsky (26) did a lot of work repeating the experiments of earlier workers in order to determine the value of their findings. Hopkins (1906) suggested that rickets was caused by a nutritive error consisting of a specific organic factor. Prof. Mellanby (1920) made the first approach in the search for an anti-rackitic vitamin in food. He said it was a fat soluble vitamin and the same as vitamin A. He used foods rich in vitamins B and C but poor in A to produce rickets; and found that cod liver oil had the strongest anti-rackitic power.

Harden and Zilva (1919) used vitamin A in determining the effect on monkeys. Tozer used guinea pigs; Makay (1921) worked with Kittens; Shipley, Park, McCollum and Simmonds (1921) used rats; and Hess, McCann and Pappenheimer also used

rats. These workers all found no ricketic change in the skeletons of the rats, when fed on a diet deficient in vitamin A, but they did find osteo-porosis. Back in 1898, Heter, who knew nothing of vitamins used four pigs to determine the value of fat free diet in causing rickets, and was not able to produce the disease (26).

Findlay (2) Patton and Watson published several papers to show that milk butter fat contained no accessory factor protecting against rickets.

Dalyell, Hume, Mackay and Smith prevented rickets by the use of cod liver oil, developing in animals fed on a diet that would produce rickets. They thought that vitamin A was the principle factor (26).

Hodgson (26) brought up the theory that rickets was due to an acidotic condition. This theory was an old one, first suggested by Leibig in 1884; Piotrowsky and Budheim in 1859 and Heiss in 1876 again brought it to the front. They explained the theory as follows: the organic acids in the blood extract the calcium from the skeleton and thus produces either rickets or osteo-porosis. They found lactic acid in the bones and urine of rickety children. In the years 1863 to 1890, Frey, Schmutzer, Hoxter, Hess and Warschauer found the opposite conditions. Hodgson in bringing up this theory again, said it was due to a reduced alkaline reserve.

Mellanby (25) used puppies for experimental work, and said that rickets could be produced more easily if skimmed milk was used; also that it could be prevented by the use of

fat soluble vitamins, cod liver oil being the best for this purpose. Lean meat had some anti-rackitic power and was thought to assist the calcium metabolism. Bread on the contrary, he said, inhibited calcification with a poor vitamin diet. Calcium alone did not produce rickets if it was deficient but it did exaggerate its effects. The anti-rickitic factor in butter was more effective if there were an abundance of calcium salts present. He found that exercise had an anti-rickitic power on puppies, depending to a large extent on the diet; but could not produce rickets even in the absence of all exercise if the diet was good.

Korenchevsky (26) after some work with Arsenic and Phosphorus reached the conclusion that: apparently a deficiency of phosphorus alone in a diet abundant in anti-rickitic factor causes no considerable change in the skeleton; and in no case produced rickets. Arsenic had a similar action to phosphorus. McCollum produced severe rickets in rats by a diet poor in anti-rickitic factor, but very rich in calcium salts, and with a reduced or sufficient amount of phosphorus.

Hansemann (1906) said rickets was due to deprivation of fresh air and exercise. He reached this conclusion after studying animals in the zoo. He also looked up the post-mortem records of children born in the spring and dying in the fall, and born in the fall and dying in the spring (26). Schmorl 1909, from post mortem records, said the worst rickets occurred in cold weather. Findlay (2) reached the following conclusions: Rickets is a disease of the temperate zone

and seldom met with in tropical or sub-tropical countries. Warm climate permits the child to be brought up out of doors, and with the houses used only for sleeping purposes. Negroes and Italians, though free from the disease in their native land, are very susceptible to rickets in New York city. Rickets is more prevalent among the poor than the rich. Children of the latter get more exercise and fresh air. And the poor are often crowded together in small rooms and the children have very little exercise until they become older."

Ferguson, Patton and Findlay (26) in 1918, in an investigation in Glasgow noted a series of facts supporting the theory that confinement and a lack of exercise are conducive to the development of rickets. They studied 200 cases of severe rickets, and 150 cases of mild rickets. They found: inadequate air and exercise seem to potent factors in determining the onset of rickets; the probability of rickets increased with the number of children in the family; the cubic feet of space was less for the large and the poor family; cleanliness was better in the non-rickitic than in the rickitic family.

Moisture as a factor in rickets was observed in Russia in those provinces where the moisture exceeds 80%. Shukowsky explained this in 1900 by the fact that the children are kept indoors more in a humid climate. Korenchevsky (26) was not able to tell any difference, in his work with rats, in different degrees of moisture.

The first effect of light on the disease was noted by

by Bucholz in 1904. In 1918, Winkler saw the favorable effects of the roentgen rays on rickets (26). Violet rays were used effectively by Haldschnisky in 1919, Putzig (1920), Karger (1920), Riedel (1920), Erlicher and Mengert (1921), Hume, Mackay and Smith in (1922). Hess, Unger and Pappenheimer prevented rickets with exposure to the light of the sun, in 1922. They used rats and exposed them 15 to 30 minutes daily to the sunlight (27).

In 1922, we see that the etiological factors of rickets are thought to be: nourishment of the mother during pregnancy, and lactation may be an important factor; increased incidence of rickets during the winter months and spontaneous cure in the summer explained by the effects of light and diet; seasonal fluctuations in incidence explained by variations in food content; light is a factor, and more of it is obtained by the child in the summer months and by the child in the warm climate; exercise, air, calcium, and vitamins are all important factors; finally, cod liver oil is the best source of anti-rickitic factor.

Beginning with 1920, experimental rickets took on new interest for many investigators. This is to a large extent due to the fact that rickets could now be produced at will in experimental animals. The past theories on rickets were difficult to prove and were supported with arguments on a clinical or academic basis. During the last fifteen years, however, the theories have been backed up by experimental results or have been refuted.

Heredity is one of the oldest supposed causes for rickets. Seigert (7) about 1905 made a study of many families in which rickets was either notably absent or present. He thought heredity the most important factor in the etiology of the disease. This would presuppose some change in the germ plasma, but there seems to be no adequate basis for this idea. On the contrary, he did not take into consideration the factors of environment, sunlight, and pigment; all of which will explain why heredity appeared to play so large a part. Today, the role of heredity is thought to be in a generic sense such as the pigment of the skin of the negro, or the environment of the individual; and the effect is thus a secondary one.

Age is an important factor (7, 28). The infant is exposed less to the sunlight, grows faster and needs more calcium and other minerals in order to build bone. Rickets is not congenital and heals itself, usually, before the fifth year. These conclusions have been reached following roentgenographical examinations of the bones of many children.

Sex, according to Fromme, was thought to be important in the incidence of rickets. He said it was much more frequent in males than females. The exact part played by sex is not yet definitely worked out, but it seems to be more of an endocrine factor in the disturbance of the calcium metabolism with the resulting tetany than in rickets itself (7).

The congenital factor has been much discussed. Kasowitz believed all cases to be congenital, basing his conclusions on histological changes in the bones; but his er-



ror in interpretation of the bone changes was later shown by several workers. Schmorl (7) took the opposite viewpoint. Hess and Weinstock (29) in a study of 250 cases of the epiphyses of the bones of new-born infants, with x-rays found no rickets. Again, by chemical analyses of the blood, by Hess and Matzner, no relationship was found between the content of calcium or of inorganic phosphorus in the blood of the newly born and the subsequent development of rickets (30). The best argument in favor of congenital rickets is probably that premature infants are almost always subject to it in some degree. Another explanation of this may be the extremely rapid rate of growth of the premature infant.

Diet, an old theory as to the cause of rickets, is still thought to play an important part. Korenchevsky (26) laid a great deal of importance to the value of the milk of the lactating animal. He said the young might be protected from rickets by the fat soluble vitamin A and the calcium content of the milk of the mother. Mellanby (31) wrote a paper showing that rickets was due to a deficiency of the fat soluble vitamin A. Further experimentation soon proved that there was an error and that animals deprived of this vitamin did not develop rickets, but rather they developed keratomalacia a disorder of the eyes (32). Hopkins (1920) showed that oxidation destroys vitamin A (33). In 1922 McCollum (34) demonstrated that what was formerly thought to be a single fat soluble vitamin was in reality two vitamins; and he separated them by means of oxidation. He sub-

jected cod liver oil to a stream of air bubbles, at the temperature of boiling water, for twelve to fourteen hours. This was used on rats to see if it would protect them from xerophthalmia and rickets. It was found that it did protect them from rickets but not from xerophthalmia, so he concluded that there was still an active principle effective against rickets and he called this vitamin D. These findings were soon confirmed by Goldblatt and Zilva (35). Thus Funk (36) was proved correct when he included rickets in a list of diseases due to deficiency of some vital factor or avitaminosis in 1914.

Hutchison and Shah (37) working with Hindus and Mohammedans in India proved fairly conclusively that vitamin A was not the anti-rickitic factor. The confusion on this point for several years seems to have been due to the separation of the fat soluble vitamins being so difficult, or to a failure to appreciate the fact that there were two fat soluble vitamins involved. Since this fact has been demonstrated, it is easy to see why there were conflicting results over the anti-rickitic power of the fat soluble vitamin. This anti-rickitic factor is not as well distributed in nature as are the water soluble vitamins. It is present to the largest extent in cod liver oil, next in the yolk of hens eggs, and in a very minimal amount in the cream of cow's milk. Now it is generally agreed that the eggs and milk depend for the amount of the factor which they contain, on the exposure

to the amount of ultra violet light that the animals or chickens were subjected.(7).

In 1919, Mellanby (38) proved by experiments with dogs that the factor in cod liver oil was a specific for rickets. Shipley, Park, McCollum and their associates demonstrated the same the same value of cod liver oil in the cure of rickets in rats (39). Experiments to determine the value of feeding cod liver oil to pregnant animals showed that there was no immunity conferred to their offspring. The same has been found true in the case of man by Hess (7). Later experiments have shown that irradiated ergosterol is a reliable specific and is effective in extremely small amounts. But there is danger with this substance in giving too large a dose for it is very toxic .

There was for some time, and still is among a few physicians and a great many of the laity, a belief that the leafy vegetables, particularly spinach, had an anti-rickitic power. Hess and Unger in 1920, found that rickets persisted in spite of a diet which included a large amount of spinach daily (40). Zucker in 1923, showed that the amount of fat soluble principle in spinach and carrots, necessary to protect against rickets, was of negligible quantity (41). McClendon (42) found no protective power in spinach to protect against rickets, but it did protect against xerophthalmia. Zilva (43) found no anti-rickitic factor in cabbage or carrots. Shipley, Kinney, and McCollum found none in extracts of spinach, brussels sprouts, cabbage, celery, tomato or sweet potato (43).

For several years some workers thought butter had some value in preventing the disease. McCollum (44) demonstrated that it was necessary to feed 15 to 20 % of butter fat in order to protect against rickets. It did have more value as a preventive measure in xerophthalmia.

Milk of mothers, although it does not have as high a percentage as that of cow's milk, is of much more importance in protecting the infant against rickets. Repeated studies have shown that the degree of incidence of rickets is less in those babies nursed by their mothers over those fed on cows milk or special baby formulas. However Hess, and Unger found almost all of the negroe babies in a certain community developed rickets even though nursed by their mothers (45). Hess and Weinstock (46) and Outhouse, Macy and Breck (47) have found by using human milk on rats, that the high power of protection it had against rickets, is not due to the anti-rickitic factor of the milk. However, Hess, Weinstock and Sherman, in 1927, Found that by irradiating the nursing mother with ultr-violet light, that the milk following this irradiation had a high power of anti-rickitic factor. This could not be done by feeding cod liver oil, but to some extent was possible by feeding irradiated ergosterol. Hart, Steenbock and their associates (49) found there was more value in the radiations from a quartz mercury-vapor lamp than from the sun's rays. Condensed milk was thought to tend to produce rickets, but this seems not to be the case (7). The same thing was

true of protein milk. Hess (7) explains this on the basis of the extremely rapid growth of the infant fed on protein milk.

Cereals have been associated with a particular type of rickets; that of the overweight, large, flabby infant, with knock-knees or bowed-legs. In 1921, Mellanby published a paper showing that it was the carbohydrate that produced the rickets, and that oatmeal, barley, rice and wheaten flour had a deleterious effect upon bone production in the order named (50). Hess, in this country, reminds us that we do not use as much oat cereal as we do wheat, and concludes that if oats is a factor, it must be a secondary one (7). Also, in most cases, cereals are not placed in the diet until about the sixth month at which time rickets is usually well developed if it is going to develop.

Hygiene, as the primary factor in the etiology, has for years been a subject for argument. In the past the pendulum has swung from one extreme to the other. Most of the arguments however were not on an experimental basis. Findlay (51) has sponsored the importance of exercise. Kassowitz (7) said that the breathing of noxious gasses in poorly ventilated rooms was the big factor. Today, there is more stress on sunlight than on fresh air, but it is impossible to the first without the second. The value of fresh air was tested by Hess by taking rats, placed on a rickets producing diet, and placing half of them out of doors at night and the other half out of

doors in the daytime to get the sunlight. The first group developed the rickets, the second group did not. This showed that the fresh air without the sunlight did not protect against rickets (7).

Huldschinsky (52) in 1919, showed the value of Ultra-violet light in connection with the etiology of rickets. He first demonstrated the curative effect of the mercury-vapor lamp by radiographs of the epiphyses of the long bones of rickitic infants. Rats were then used to determine the wave length best fitted to cure the disease. Hess and his workers showed the difference in the amount of radiation needed to protect white and black rats. More radiation is needed to protect the black rats than the white rats (7). Originally it was thought that the value of ultra-violet light was in elaborating vitamin A. Sheets and Funk (53) soon demonstrated that these rays had an effect only upon the anti-rickitic factor and not on the vitamin A or anti-xerophthalmia factor. In 1921, Hess and Unger (54) demonstrated the curative effect of sunshine on rickets. About this time rickets was able to be produced in rats by means of a diet deficient in Phosphorus. Powers and Park (55) and Hess, Unger and Pappenheimer (54) found that the radiations of the mercury-vapor lamp were as effective in curing the disease in rats as it was in infants. Then in 1925, Hess and Weinstock (29) took some excised human skin, and after irradiating it with the mercury-vapor lamp, found that it also conferred immunity against

rickets,,when fed to the rats. The skin not irradiated did not confer any immunity. These experiments at first were interpreted to mean that the active substance was cholesterol. The next few years, however, proved that it was not cholesterol but rather ergosterol. Hess (56) and Steenbock (57), in 1924, used the rays from the mercury-vapor lamp to produce the anti-rickitic factor in different foods; particularly in vegetable oils and milk. Very little of the anti-rickitic radiations will pass through clothing. But on the other hand, very little of the skin need be exposed to give sufficient ergosterol to protect the infant from the disease. This fact is in keeping with what we know of the extreme potency of activated ergosterol.

The seasonal variation of rickets has for a long time been noticed by clinicians, but not until the action of the ultra-violet radiations of the sun were known, was this fact understood. In 1922, Hess and Lundagen (58), experimenting with the phosphate of the blood, noticed a periodic alteration according to the season. There was a lowered blood phosphate in the winter time and an abundance of blood phosphate in the summer time. Many experiments, with the value of the sun's rays in protecting against rickets, by different experimentors, seems to point out that it isn't so much the amount of the sunlight as it is the quality and intensity of the sun's rays. Hess (7) sums up the knowledge of the action of the ultra-violet rays as follows: "Now it has been

actually proved, although formerly it had been suggested by many, that actinotherapy is the result of a photochemical reaction upon a definite substance."

Fehling, in 1887, proposed a theory that osteomalacia was due to an overactivity of the ovaries (59). Since that time there has been a strong tendency on the part of many writers to try to place rickets on an endocrine basis. There appears to be a definite relationship between tetany and the parathyroid glands. Osteomalacia is extremely more frequent in pregnant women as compared to non-pregnant women. These phenomena would seem to indicate a relation between the parathyroids and disturbances of the skeleton. In the case of rickets, the calcium and phosphorus content of the blood is raised following the ingestion of small amounts of irradiated ergosterol. Hess, Lewis and Rivkin (60), working with normal infants, have shown that the calcium content of the serum may rise to a level as high as 15 or 16 mg. With this hypercalcemia there goes a hypercalcification of the epiphyses of the long bones. Irradiated ergosterol was fed to animals suffering with a low calcium type of rickets and the serum calcium rose at once, but after the parathyroids had been removed, no benefit was obtained; the signs of tetany were not allayed, nor was the calcium of the blood serum increased very much. These facts would point to a relationship of an action of the irradiated ergosterol on the parathyroids and not of a direct action on the serum calcium content.



Park and McClure(61) thought that they had produced rickets by extirpation of the thymus, but the value of these as well as of many other workers is negligible in the light of the temporary effect which was produced. Steelzner had claimed that adrenalin was of value in the treatment of rickets, but Hess and Jaffe (62) failed to find this the case in their extirpation experiments of the adrenals of rats. Work of many men trying to show the relation of rickets and other of the endocrine glands have so far been unsuccessful.

The Italian Physiologist, Morpurgo, brought out the theory that an infection was the basis of rickets. He carried out many experiments with rats, by innoculating them with bacteria, to produce what he thought was rickets. In 1911, Kock (63) came to the same conclusions after working with dogs, but the value of his work was lessened due to the artificial methods. He had injected the bacteria directly into the epiphyseal line and an enlargement of the line resulted. This would in any case result due to disturbing the cells, and the result was not a clinical picture of rickets either. Kassowitz (64) claimed that frequent attacks of pneumonia or other respiratory infections tended to cause rickets. Hess (7) was unable to verify this claim. Syphilis was an early suspect for the cause of rickets. First Boerhave, and more recently Parrot, Fournier and Marfan have taken this view (65). Other workers, particularly in this country, have been unable

to take this attitude. Marfan (66) also said that tuberculosis was a cause. He explained his position on the basis of the changed marrow and cartilage. But he also had other changes extending to the adenoid tissue and lymphatic glands. The part played by toxins is difficult to ascertain. One thing is true of all this type of experiments however, and that is the atypical picture which results.

Phosphorus now plays an important part in the production of experimental rickets. In view of the fact that 95% of the calcium in the bones exists there in the form of the phosphate, it is rather surprising that attention to the phosphate ion was not given earlier. It is true that Heubner in 1909, published an investigation to this fact (67). But not much attention was paid to this until 1921, when Sherman and Pappenheimer and McCollum, Park and Shipley announced that they had produced rickets by a deficient phosphorus ration (68), (69). Stæltzner, in 1908, reported that he had produced rickets, characterized by an excessive production of osteoid, by feeding strontium (70). Since that time this fact has been confirmed several times. Lehnerdt (71) fed diets, high in strontium content, to puppies and rabbits, and also to dogs suckling their young and produced it in the pups. Shipley and Park confirmed the work of Lehnerdt, and noticed that the abnormal histological structure could not be prevented by the giving of cod liver oil (72). Hess (7) also states that these animals can neither be protected by liberal

amounts of irradiated ergosterol. So far this condition of an increased strontium content has not been of much clinical significance as it seems to be only an artificial condition.

In glancing briefly through the history of rickets, as we have done, we see that it is roughly divided into four periods. The first period extends from the earliest references of similar syndromes down to the time of Glisson in 1650. The high lights of this period were the references to this clinical syndrome in Rome in the second century A. D. by Soranus of Ephesus. Galen and Hippocrates both fail to describe a disease which without doubt referred to rickets. It was thought by Soranus to be due to the immoral practices of the Roman women at the time of conception. Several paintings of the sixteenth century show typical signs of rickets. In the first part of the seventeenth century there were several references to the clinical picture of rickets, mostly by Frenchmen.

Glisson in 1650 gives a very good account of the disease and states definitely that it appeared in England in the beginning of that century. He attributes the disease as due to the soft living condition of the south country where it was most prevalent. He said it was not a congenital disease but due to environment and that a loose effeminate constitution in either parent, an overmoist and full diet and a sedentary and soft life were the causes. For the next two hundred and fifty to three hundred years little was done to add new light

to the subject of etiology. Numerous theses were written about it but they followed Glissons idea of the cause. In 1885, Bommer contributed quite a little to the understanding of rickets with his work on the histological pathology. And Little helped clear the coception of rickets as differentiated from Cretinism.

Following this work the medical profession took a new interest in the disease and began to experiment. Animals were now used to experiment with and it was soon found that it was fairly easy to produce rickets in the rat. The vitamin theory stimulated many workers and at first it was thought that the fat soluable vitamin A was the factor. Many writers said it was an environemental thng and laid great stress on diet, while others said fres air and exercise was the thing.

After 1918 we have the beginning of the present period. The fat souable factor was divided by oxidation in to two factors. The value of the ultra violet rays was established. The therepeutic value of cod liver oil was demonstrated, and the potency of irradiated ergosterol was established. The part played by fresh air and exercise is now seen by all. The roentgen rays as a means of diagnosis and of progress helped a great deal and is still our most useful means of detecting early rickets. The exact relationship of the endocrine system to the disease is not yet thoroughly understood. But today we know much of the cause and have a valuable agent for its cure and prevention. Cod liver oil, the ultra violet rays,

irradiated ergosterol and much later food substances and animal products, irradiated with ultra violet rays, especially milk, give us adequate material for curing and preventing the disease.

The History of Rickets, then we see, bears out the phrase: "Understanding of a disease is essential for then the cure and prevention follow closely in its wake.

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## BIBLIOGRAPHY

- (1) Dick, J. Lausen: History Of Rickets  
W. Heinmann, London, 1922.
- (2) Findlay, Richard F.: Social and Economic Factors in  
the Causation of Rickets,,an introductory hist-  
orical survey. London, 1918.
- (3) Smith, G. E.: Archeological Survey of Nubia, Cairo,  
II, 1914.
- (4) Ruffer, A.: Study of Ancient Egyptian Teeth, Amer.  
Jour. Phisic. Anthrep., 1920, 3, 335.
- (5) Dick, John Lausen: Rickets: a study of economic con-  
ditions and their effects on the health of the  
nation, London, W. Heinmann,Ltd., 1922.
- (6) Findlay, Leonard: ,: A study of Social and Economic  
Factors in the Causation of Rickets, by Marg-  
aret Ferguson with an introductory survey by  
Leonard Findlay,London, 1918.
- (7) Hess, Alfred F.: Rickets, Osteomalacia and Tetany,  
Lea & Ferbiger, Philadelphia, 1929.
- (8) Garrison, Fielding H.: An Introduction to the History  
of Medicine, W. B. Saunders, Philadelphia and  
London, 1929.
- (9) Hess, Alfred F.: Rickets, Osteomalacia and Tetany,p 23,  
Lea & Ferbiger, Philadelphia, 1929.

- (10) Ebstein, W.: Ueber Das Vorkommen rachitischer Skel-  
ettveraenderungen im Altertum und im Mittelalter,  
Virchow's Archive, 1908, 193, 519.
- (11) Foote, J. A.: Evidences of Rickets Prior to 1650,  
Amer. Jour. Dis. Child., 1927, 34, 443.
- (12) Guillimeau, J.: Child-birth or the Happy Delivery of  
Women. To which is added a Treatise of the Disease  
of Infants and Young Children with the Cure of  
Them, London, 1612.
- (13) More, N.: The History of the First Treatise on Rickets,  
St. Bartholomew's Hosp. Reports, London, 1884.
- (14) Fuller, Thomas: Good Thoughts in Bad Times and Other  
Papers, 1647. Reprinted by Ticknor and Fields,  
Boston, 1863.
- (15) Barlow, Sir Thomas: Keeling's Cyclopedia of Diseases  
of Children, Vol. II.
- (16) Burland, Charles; An Historical Case of Rickets; an A  
account of the remains of Princess Elisabeth, by  
the late E. P. Wilkinson, Practitioner, Vol. Ioo  
1918.
- (17) Mayow, J.: De Rachitide, London 1669. The Mother's  
Family Phisician or the Infants Doctor. Being  
a Discourse of the disease in Children Commonly  
Called the Rickets, Oxford, 1687.
- (18) Hess, Alfred F.: Rickets, osteomalacia and tetany, p24,  
Lea & Ferbiger, Philadelphia, 1929.

- (19) Wendelstadt, G.: Die endemische Krankheiten Wezlar's, Neues J. d. prakt. Arzneykunde, 1801, 12, 90.
- (20) Trousseau, A. et Lasèque, C.: Du Rackitisme et de l'osteomalacie comparés, Arch. gener. de med., 1849, 19, 257.
- (21) Pommer, G.: Untersuchungen über Osteomalacie und Rackitis, Leipzig, 1885. F. C. W. Vogel.
- (22) Little, William John: Medical and surgical aspects of in-knee (genu-valgum) its relation to rickets, its prevention, and its treatment without surgical operation. New York, D. Appleton & Co. 1882.
- (23) Garrison, Fielding H.: An Introduction to the History of Medicine, W. B. Saunders, Philadelphia and London, 1929. p. 877.
- (24) Medical Research Council (Gt. Brit.); Studies in Rickets in Vienna 1919-1922, London, H. M. Stationery off., 1923.
- (25) Mellanby, Edwards: Experimental Rickets, London, H. M. Stationery off., printed by F. Hall, at the University press, Oxford, 1921.
- (26) Kerenchevsky, V.: The Etiology and Pathology of Rickets from an Experimental Point of View, London, H. M. Stationery off., 1922.
- (27) Hess, A. F., Unger, L. J., Pappenheimer, A. M.: The Prevention and Cure of Rickets by exposure to Sunlight, Proc. Soc. Exper. Biol. and Med., 1921, 19, 8.



- (28) Schmorl, G.: Discussion, Verhandl. Deutsch. path. Gesell., 1908, II, 286.
- (29) Hess, A. F., Weinstock, M.: A Study of Light Waves in Their Relation to Rickets, Jour. Am. Med. Assn., 1923, 80, 687.
- (30) Hess, A. F., Matzner, M. J.: Rickets in Relation to the Inorganic Phosphates and Calcium in Maternal and Fetal Blood, Amer. Jour. Dis. Child., 1923, 26, 285.
- (31) Mellanby, E.: Experimental Rickets, Med. Reserch Council, Special Report No. 61, London, 1921.
- (32) Hess, A. F., McCann, G., Pappenheimer, A. W.: The Failure of Rats to Develop Rickets on a Diet Deficient in Vitamin A., Jour. Biol. Chem., 1921, 47, 395.
- (33) Hopkins, F. Gowland: Effects of Heat and Aeration Upon the Fat-soluable Vitamin, Bioch. Jour. 1920, 14, 725.
- (34) McCollum, E. V., Simmonds, N., Becker, J. E.: An Experimental Demonstration Of the Existence of a Vitamin which Promotes Calcium Deposition, Jour. Biol. Chem., 1922, 53, 293.
- (35) Goldblatt, H., Zilva, S. S.: Effect of Heat on Growth-promoting Antirackitic Substances, Lancet, 1923, ii, 637.
- (36) Funk, C.: Die Vitamine, ihre Bedeutung fuer die Physiologie und Pathologie etc., J. F. Bergmann, Wiesbaden, 1914.

- (37) Hutchison, H. S., Shah, S. J.: The Etiology of Rickets, Early and Late, Quart. Jour. Med., 1922, 15, 167
- (38) Mellanby, E.: The Present State of Knowledge Concerning Accessory Food Factors, Med. Research Com. Report No. 38, 1919.
- (39) Shipley, P. G., Park, E. A., McCollum, E. V.; Simmonds, N., Parsons, H. T.: The Effect of Cod-liver Oil Administered to Rats with Experimental Rickets, Jour. Biol. Chem., 1921, 45, 343.
- (40) Hess, A. F., Unger, L. J.: The Clinical Role of the Fat Soluble Vitamin. Its Relation to Rickets, Jour. Amer. Med. Assn., 1920, 74, 217.
- (41) Zucker, T. F., Barnett, M.: Observations on the Distribution of Antirachitic Substances, Pro. Soc. Exper. Biol. and Med., 1923, 20, 375.
- (42) McClendon, J. F., Shuck, C.: The Presence of Antiophthalmic Vitamin and the Absence of Antirachitic Vitamin in Dried Spinach, Soc. Exper. Biol. and Med., 1923, 20 288.
- (43) Shipley, P. G., Kinney, E..M., McCollum, E. V.: The Effect of Certain Extracts of Plant Tissues on Florid Rickets, Jour. Biol. Chem., 1924, 59, 165.
- (44) McCollum, E. V., Simmonds, N., Becker, J. E., Shipley, P. G.: An Experimental Demonstration of the Existence of a Vitamin which Produces Calcium Deposition, Jour. Biol. Chem., 1922, 53, 293.

- (45) Hess, A. F., Unger, L.J.: Prophylactic Therapy for Rickets in a Negro Community, Jour. Am. Med. Assn., 1917, 69, 1538.
- (46) Hess, A. F., Weinstock, M.: A Comparison of the Evolution of Carpal Centers in White and Negro New born Infants, Amer. Jour. Dis. Child., 1925, 29, 347.
- (47) Outhouse, J., Macy, I. G., Brekke, V.: Human Milk Studies V. A Quantitative Comparison of the Antirachitic Factor in Human Milk and Cow's Milk, Jour. Biol. Chem., 1928, 78, 129.
- (48) Hess, A. F., Weinstock, M., Sherman, E.: Antirachitic Properties Developed in Human Milk by Irradiating the Mother, Jour. Amer. Med. Assn., 1927, 88, 24.
- (49) Hart, E. B., Steenbock, H., Elvehjem, C. A., Scott, H.: The Influence of Sunlight upon Calcium Equilibrium in Milking Cows, Jour. Biol. Chem., 1926, 67, 371.
- (50) Mellanby, E.: The Effect of Cereals and their Interaction with other Factors of Diet and Environment on Producing Rickets, Med. Research Council, Special Report No. 93, London, 1925.
- (51) Findlay, L.: Etiology of Rickets, Lancet, 1922, 1, 825.
- (52) Hulschinsky, K.; Die Behandlung der Rachitis durch Ultraviolettbestrahlung, Ztschr. f. orthop. Chir., 1919, 1920, 39, 426.
- (53) Sheets, O., Funk, C.: The Effect of Ultra-violet Rays on Rats Deprived of Vitamin A., Proc. Soc. Exper. Biol. and Med., 1922, 20, 80.

- (54) Hess, A. F., Unger, L.J., Pappheimer, A. W.: The prevention of Rickets in Rats by Exposure to Sunlight, Proc. Soc. Exper. Biol. and Med., 1921, 19, 8; Jour. Biol. Chem., 1922, 50, 77.
- (55) Powers, G. F., Park, E. A., Shipley, P. G., McCollum, E. V., Simmonds, N.: The Prevention of the Development of Rickets in Rats by Sunlight, Proc. Soc. Exper. Biol. and Med., 1921, 19 43.
- (56) Hess, A. F.; The Experiments on the Action of Light in Relation to Rickets, Proc. Am. Pediat. Soc., June 7, 1924, 36,.
- (57) Steenbock, H., Black, A.: Fat-soluable Vitamins. XXIII. The Induction of the Growth-promoting and calcifying Properties in a Ration by Exposure to Ultra-violet Light, Jour. Biol. Chem., 1924, 61, 405.
- (58) Hess, A. F., Lundagen, M. A.: A Seasonal Tide of Blood Phosphate in Infants, Jour. Am. Med. Assn., 1922, 79, 2210.
- (59) Fehling, H.: Zehn Castrationen ein Beitrag nach dem Werthe der Castration, Arch. f. Gynak., 1884, 22, 441.
- (60) Hess, A. F., Lewis, J. M., Rivkin, H.: Clinical Experience with Irradiated Ergosterol, Jour. Amer. Med. Assn., 1928, 91, 783.
- (61) Park, E. A., McClure, R. D.: The Results of Thymus Ex-terpation in the Dog, Am. Jour. Dis. Child., 1919, 18, 317.

- (62) Hees, A. F., Jaffe, H. L.: The Effect of Double Adrenalectomy on the Development of Rickets in Rats, Pro. Soc. Exper. Biol. and Med., 1924, 22, 103.
- (63) Kock, J.: Untersuchungen über die Lokalisation der Bakterien, das Verhalten des Knochenmarkes und die Veränderungen der Knochen, insbesondere der Epiphysen bei Infektionskrankheiten, Mit Bemerkungen zur Theorie der Rachitis, Ztschr. f. Hyg., 1911, 69, 436.
- (64) Kassowitz, M.: Die normale Ossifikation und die Erkrankungen des Knochensystems und hereditären Syphilis; Wien, Braumueller, 1881-1885. Also: Gesammelte Abhandlungen, etc., Berlin, 1914.
- (65) Parrot, J.: La syphilis hereditaire et le rachitis, Paris, Treisier, 1886. The Osseous Lesions of hereditary Syphilis, Lancet, 1897, i, 696.
- (66) Marfan, A. B.: Maladies des Os, Paris, 1912.
- (67) Heubner, W.: Versuche über den phosphorumsatz des wachsenden Organismus, Verhand. d. Gesellsch. f. Kinderheilk., 1909, 36, 149.
- (68) Sherman, H. C., Pappenheimer, A. M.: A Dietetic Production of Rickets in Rats and its Prevention by an Inorganic Salt, Proc. Soc. Exper. Biol. and Med., 1921 18, 193.
- (69) Shipley, P. G., Park, E. A., McCollum E. V., Simmonds, N.: The Effects on Growing Rats of Diets Deficient in Calcium, Am. Jour. Hygiene, 1921, 1, 492.

- (70) Stoeltzner, H.: Ueber den Einfluss von Strontiumverfuetterung auf die chemische Zusammensetzung des wachsenden Knochens, Bioch. Ztschr., 1908, 12, 119.
- (71) Lehnerdt, F.: Zur Frage der Substitution des Calciums um Knochensystems durch Strontium, Beitrage z. path. Anat. und allgem. Path., 1910, 47, 215.
- (72) Shipley, P. G., Park, E. A., McCollum, E. V., Simmonds, N., Parsons, H. T.: The Effects of Strontium Administrations on the Histological Structure of the Growing Bones, Johns Hopkins Hosp., Bull. 1922, 33, 216.